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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,909	05/04/2001	R. John Collier	00742/060002	7132

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/848,909	COLLIER ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Feb 11, 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,43,44,49 and 52-64* is/are pending in the application.

4a) Of the above claim(s) *43,44 and 49* is/are withdrawn from consideration.

5)☒ Claim(s) *6 and 56-64* is/are allowed.

6)☒ Claim(s) *1 and 52-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,6,43,44,49 and 52-64* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1 and 6 have been amended.

Claims 2-5, 7-42, 45-48, and 50-51 have been canceled.

Claims 43-44, 49 stand withdrawn from consideration.

New claims 52-64 have been added.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 11, 2004 has been entered.

Allowable Subject Matter

2. Claims 6, and 56-64 define over the prior art of record and therefore define subject matter that is allowed.

Rejections Withdrawn

3. Claims 1, 6, 12 and 33 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-6, and 7 of U.S. Patent No. 6,455,673, in light of the amendment of claim 1 to recite a non-obvious species of invention, and cancellation of claims 12 and 33.

Claims 1,6,8,12,15 and 33 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims1-13 and 23-27 of U.S. Patent No. 5,917,017, in light of the amendment of claim 1 to recite a non-obvious species of invention, and cancellation of claims 8,12,15 and 33.

4. Claims 6-8, 33-35 and 42,45-47 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immunogenic compositions, and site directed mutants of PA63 for the induction of a protective immune response, does not reasonably provide enablement for the use of any mutant toxin as a pharmaceutical composition (vaccine). The specification does not enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to use the invention commensurate in scope with these claims, has been obviated in light of the cancellation and amendment of the claims.

5. All prior art rejections over Collier, Cirino, Johnson, Singh, Miller and Collier are herein withdrawn in view of the cancellation of claims and amendment of others to obviate the applied references.

6. Claims 1,3,6,12,15-18, 33, 40-41,47, 50-51 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention set forth in paragraph 50, page 20, dated August 4, 2003 has been reformatted below to address the new combination of claim limitations as well as many of the claims have been canceled.

7. Claims 1,12,30,33,40-41 and 47 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, has been obviated through cancellation of claims, and amendment of claim 1.

New Claims and Claim Limitations/New Grounds of Rejection

Please Note: The following rejections are being made of record over the newly amended or submitted claims based upon the reading of the claims as follows:

Definitions for:

Moiety: originally, a half, loosely, a portion of something; functional group (Stedman's)

:a component part of a complex molecule (Drug Discovery & Development)

:also any part or portion (Dorland's Medical Dictionary)

Amended claim 1 is directed to moieties with no required biological function, and must comprise any amino acid sequence of SEQ ID NO 8 that shares 95% identity with SEQ ID NO 8, and includes that D425K mutation. Within the scope of claim 1 is a moiety that comprises D425K. Claim 1 does not require the moiety to evidence any specific biological function but must only comprise an amino acid sequence with 95% identical to a reference sequence of SEQ ID NO 8

Reference SEQ ID NO 8 (735 aa): ----------

Scope of what is Claimed:

Comprises 100% identity to an amino acid sequence of SEQ ID NO 8 specifically: D425K,

XXXXXXXXX - (D425K) XXXXXXXXXXXXXXXXXXXXX

Or "ie. 5 differences for every 95 aa identical and must include (D425K)

X" different aa: XXXXX ----------

X----------X----------X----------XX----------

X----------XXXX----------

---------XXX----------XX----------

At paragraph [0013] of the instant specification, the invention is defined to include a moiety that evidences a deletion mutation of "at least 20 amino acids of the residues in the D2L2 loop of PA", a complete deletion of "all or part of the D2L2 loop and a deletion of amino acids that are N-delta or C-terminal to the loop", thus defining the claimed moiety to comprises only the required amino acid sequence of D425K and may evidence any biological function and structure that includes the D425K mutation.

8. Claims 1, 52-55, as previously applied to claims 1-4,6-8,12-120,33-35,40-41,47,50-51 rejected under 35 U.S.C. 112, first paragraph, (written description) as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amended and new claims are directed to B-moieties that comprise a portion or fragment of the an amino acid sequences set forth in the reference sequences, such as SEQ ID NO 8, 10, 11, 13, or 16 , and include specific mutations set forth in the claims.

All of the B-moieties claimed are not required to evidence any specific biological activity, and no specific sites for the additional mutations, which may include insertions, additions, deletions, and substitutions are set forth in the claims. The prior art teaches (see Blaustein, RO et al, 1989) that each portion of anthrax toxin is not toxic by itself but must be combined with an additional portion in order for toxicity to be produced, therefore the recitation of the term "anthrax toxin" set forth in the claims, defines a starting material from which the B-moiety is derived.

Original descriptive support for the instantly claimed genus of B-moieties that comprise the recited mutation sites D425K, K397D, K395D, D426K, F427A and/or deletion of amino acids 302-325, and comprises "an amino acid sequence that is 95% identical to" the reference amino acid sequence and evidences any type of biological function, to include toxicity does not evidence original descriptive support in the instant specification.

No mutant B moieties for alpha hemolysin from Staphylococcus, aerolysin form Aeromonas hydrophilia, alpha toxin from Clostridium septicum, cytotoxoin from Pseudomonas aeruginosa, hetero-oligomeric toxins (A-B5 toxins) or in the B moieties of tetanus or diphtheria toxins, as well as other oligomeric virulence factors ranging from toxins to adhesions (instant specification bridging pages 21-22) are specifically described. While Applicant has provided written descriptive support forth clostridial and Bacillus mutant B-moieties in Table 6, and SEQ ID NO 1-18, the specification does not describe mutant B-moieties from Staphylococcus,

Aeromonas, hetero-oligomeric toxin, and the genus of proteins known as toxins and oligomeric adhesions, and B-moieties that comprise any size amino acid sequence or any amino acid sequence taken from the reference sequences in any order, as the claimed products have not been described by structure correlated with function. The instant Specification, at page 22 top of page, invites experimentation to identify additional mutant B-moieties, and dominant negative forms of other oligomeric virulence factors, ranging from toxins to adhesins. An invitation to experiment, does not show possession of the genus of B-moieties that only comprise a conserved amino acids sequence; the sequence held in common not being any consecutive number or range of amino acids from the reference sequences of the claims that would define a conserved biological function .

Possession of a screen to identify mutant B-moieties for a functional characteristic, does not show possession of show possession of a highly variable genus of B-moieties of any type of biological function, that may or may-not be detected in the screen disclosed in the instant specification. No specific distinguishing characteristics are set forth in the claims to show that the B-moieties are characteristic anthrax toxin B-moieties. The genus of moieties that correspond to anthrax toxin B-moieties are clearly within the scope of the claims, as now presented and defined in the instant Specification, but original descriptive support over the highly variable genus that only shares "an amino acid sequence" of any size with the reference SEQ ID NO, and the additional mutational site or sites, and which do not evidence any specific biological function has not been described . Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The composition itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993)

and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Also see Office Action paper dated August 4, 2003, page 20.

Claim Rejections - 35 USC § 112

9. Claim 1, and 52-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 52-55 recite the phrase "an amino acid sequence"; the term "an" is an indefinite article, and does not set forth what the amino acid sequence that evidences the recited percent identity with SEQ ID NO 8. The claimed moiety is not required to comprise the entire amino acid sequence of SEQ Id NO 8, and includes fragments, and portions of SEQ IDNO 8 through the recitation of the term "moiety (see dictionary definition of moiety above)" , but must only comprise, for example, position 425 lysine through the positive recitation of D425K. Based upon the sequence listing provided in the instant Specification, position 425 of SEQ ID No 8 is K, therefore comprises 425K. Why is the recitation of D425K in the claims required when the sequence of SEQ ID NO 8 already comprises 425K? How much of SEQ ID NO 8, which contains 735 amino acids has been deleted, modified or changed? This rejection could be obviated by amending the claims to recite the phrase -------- wherein the B-moiety is 95 % identical to the amino acid sequence of SEQ ID NO 8 and position 425 is lysine --------

Claim Rejections - 35 USC § 102

10. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Kim et al (March 2000)

Kim et al disclose a mutant moiety that comprises "D425K" (see abstract, page 6175), and therefore comprises an amino acid sequence of at least 95 % identity with SEQ IDNO 8, the sequence held in common being position 425, specifically D425K. The moiety of Kim et al comprising D425K, this sequence sharing 100% sequence identity with an amino acid sequence of SEQ ID NO 8.

The moiety of Kim et al evidences loss of ability to transport molecules into a cell, and therefore meets the definition of a species of moiety of the instant invention which includes moieties that have modified biological function, the mutation being one that inhibits or abolishes internalization of a molecule into a nerve cell.

Kim et al anticipates the instantly claimed invention as now claimed.

Conclusion

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Baillie (US Pat. 6,297,966) is cited to show anthrax compositions (see all claims); Blaustein et al (1989) is cited to show anthrax toxin comprising three separate proteins, each of which is not toxin by itself (see abstract); Sellman et al (2001) is cited to show the anthrax 2B10-2B11 loop; Sellman et al (2001) is cited to show dominant negative mutants of anthrax toxin; Wesche et al (1998) is cited to show transmembrane mutants of anthrax protective antigen (B-moiety).

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on 7:30-5:00 M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
May 18, 2004

L. F. Smith

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